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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,521	08/23/2002	Mikael Simons	100564-00111	7321

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EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,521	SIMONS ET AL.	
	Examiner	Art Unit	
	Traviss C. McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,22 and 24-42* is/are pending in the application.

4a) Of the above claim(s) *9-12 and 32-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,13-19,22,24-30,41 and 42* is/are rejected.

7)☒ Claim(s) *31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

The Amendment filed December 22, 2004 has been received, entered into the record, and carefully considered. The status of the claims is as follows:

Claims 1-2, 9-12, 14-19, and 30 have been amended.

Claims 20-21, and 23 are canceled.

Claims 32-40 are withdrawn.

Claims 41-42 have been added.

Remarks drawn to rejections of Office Action mailed September 22, 2004 include:

112 2nd paragraph rejections: which have been overcome by applicants' amendments and have been withdrawn.

103(a) rejections: which have been overcome by applicants amendments and have been withdrawn.

An action on the merits of claims 1-19, 22, 24-31, and 41-42 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Newly amended claims 9-12 are directed to inventions that are independent or distinct from the invention originally filed for the following reasons: the claims originally filed were drawn to a method of modulating the sphingolipid-cholesterol microdomains in a patient, claim 9

as amended is drawn to a method of modulating the sphingolipid-cholesterol microdomains which changes membrane transport, signal transmission, cell adhesion properties, and/or enzymatic processes in a patient; claim 10 as amended is drawn to a method of modulating the sphingolipid-cholesterol microdomains which changes the proteolysis of the amyloid precursor protein of Alzheimer's disease or modifies a prion protein in a patient; claim 11 is drawn to a method of modulating the sphingolipid-cholesterol microdomains which prevents phagocytosis of bacteria and parasites in mammalian cells; and claim 12 is drawn to a method of modulating the sphingolipid-cholesterol microdomains which prevents the uptake of viruses into mammalian cells and/or their transport or release. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 9-12 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. It is noted that these claims were originally examined because they were objected to for not further limiting the claim from which they depended. The requirement that the methods of claims 9-12 additionally must change membrane transport, change the proteolysis of the amyloid precursor protein in Alzheimer's patients, prevent the phagocytosis of bacteria, or prevent viral uptake would indeed require further search and consideration, as a reference teaching modulating the sphingolipid-cholesterol microdomain may not teach or make obvious applicant's requirements of claims 9-12. As set forth supra, since applicant has received an action on the merits for the originally presented invention, claims 9-12 have been withdrawn from consideration as being directed to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 13-19, 22, 24-30, and 41-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of cholesterol sulfate, GM_1 or bbG, does not reasonably provide enablement for the use of the broad list of compounds as set forth in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Claim 1 is drawn to a method of modulating the sphingolipid-cholesterol microdomain in a patient by administering various substituted gangliosides or cholesterol derivatives. Claim 2 is drawn to a method of influencing the location of components on the sphingolipid-cholesterol microdomain by administering various substituted gangliosides or cholesterol derivatives. Claims 3-6 provide that various proteins are effected by the method of claim 2. Claim 7 provides that one of various gangliosides are administered. Claim 8 provides that a cholesterol derivative is administered. Claim 13 provides that a ganglioside is administered. Claim 15 provides that 3-30 mg of active agent are administered. Claims 16-19, 22, 24-25, and 30 provide various gangliosides which are to be administered. Claims 26-29 provide various cholesterol derivatives which are to be administered. Claims 41-42 limit the oligopeptide of claim 1.

The state of the prior art

Sphingolipid-cholesterol microdomains, or rafts, are known in the art to be lateral arrangements of specific lipids (including sphingolipids, gangliosides and cholesterol) and also include proteins and other agents (see Simons et al., Nature, vol 387, 1997, 569-72).

The level of predictability in the art

The examiner acknowledges the probability and predictability that certain agents, such as cholesterol sulfate, GM_1 and bbG have efficacy as the active agent, however the art is silent with regard to the predictability of any of the claimed gangliosides or cholesterol derivatives as claimed have the efficacy as instantly asserted, especially in view of the fact that Rietveld et al. shows that cholesterol itself had opposite effects as applicants did.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written. The examiner notes, there has not been provided sufficient instruction or sufficient methodological procedures to support the alleged efficacy instantly asserted using a compound from the broad group of the independent claims.

The existence of working examples

The working examples set forth in the instant specification are directed to the use of gangliosides BB_1 and bbG and the cholesterol derivative cholesterol sulfate. There has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples as correlative proof that any compound as claimed would indeed provide the efficacy as instantly asserted.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use of any of the broad recitation of compounds in the methods as asserted without undue experimentation. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation. One skilled in the art would be confronted with an undue burden of experimentation to isolate/manufacture, characterize, and test the various compounds of the claims to determine if indeed they have efficacy as asserted.

Applicant's defining "derivative" in the claims is seen to overcome the previous indefinite rejection for claims with "derivatives".

Claims 1-8, 13-19, 22, 24-30, and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly amended claim 1 provides that a ganglioside or cholesterol derivative selected from the group consisting of "cholesterol thiosulfate, **cholesterol molecules derivatized on the OH function**, and **cholesterol to which organic groups are added or substituted** which is formed from cholesterol in only one reaction step", which is seen to be indefinite. It is unclear as to what is to be derivatized on the OH function, and where the organic groups listed are intended to be substituted on said cholesterol molecule. One of skill in the art would not be able to determine the metes and bounds of the claim as there is no indication of what is to be derivatized on the OH function, nor where the organic molecules are to be added. Newly amended claims 2, 15 is rejected for the same reasons.

All claims which depend from an indefinite claim are also indefinite. ***Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).***

Conclusion

Claim 31 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art is not seen to teach or fairly suggest a method of

modulating the sphingolipid-cholesterol microdomain in a patient by administering cholesterol sulfate in an amount effective to increase the detergent solubility of the proteins associated with the sphingolipid-cholesterol microdomain. The closest prior art is seen to be Rietveld et al. who teaches the administration of cholesterol, which has an effect of stabilizing the microdomains.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
March 21, 2005

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623